Implantation of Rat Vascular Access Buttons in GöTTINGEN MINIPIGS
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Introduction:

Infusion and serial blood sampling are often important technical aspects of an experimental design. Subcutaneous vessels in the minipig are few and frequently accessing them is a challenge. Although minipigs have a convenient size for handling, restraint and venipuncture can be stressful and affect blood parameters. Therefore, when experiments require infusion or frequent blood sampling, catheterization is often the best option, both ethically and scientifically. The implantation of Vascular Access Ports and Selkreg Catheters is described and published in various variations. To add another option when choosing the optimal study design, we tested the Rat Vascular Access Button™ in Göttlingen Minipigs. The button allows up to three catheters to be connected and opens the possibility to sample and dose via one device but through different catheters. This has, to our knowledge, not been done before.

Material and Methods:

Three studies were conducted:

1. Pilot
   Proof of concept, determine best approach and type of catheter.
   4 male Göttlingen Minipigs (14-15 kg). Rat Vascular Access Buttons (Intech Laboratories, Inc., USA) with three ports for three catheters. Each Minipig had three catheters implanted from a midline incision:
   - In the left carotid artery, two Minipigs in cranial direction and in two caudal direction. A 3Fr PU catheter, with a beak at 3 cm was inserted to that length and fixed with a purse string suture and tissue glue. (red)
   - In the left internal jugular vein. This vessel runs alongside the carotid artery. It was ligated and a 3Fr PU catheter, with two lateral perforation holes, at 3 cm and 2 mm apart was inserted to a length of 78 cm, so the tip rested in the vena cava. (blue)
   - In the right internal jugular vein. A 3Fr PU catheter, was inserted in the same manner as in the other vein. (yellow)

   All catheters were tunneled to a subcutaneous pocket created behind the left ear and then connected to the button. The incision of the implantation site was closed in three layers, anaesthesia discontinued and the minipigs left to recover. After one week of post op care, including antibiotics and analgesia, vascular access was tested. In group housing study the animals were euthanized after that period. For a period of two or three months the buttons were accessed roughly every 7 days to test patency and functionality. At the end of that period the animals were sacrificed, and a necropsy of the affected area performed.

2. Housing
   Feasibility test of Group housing
   4 male Göttlingen Minipigs (17–20 kg). Rat Vascular Access Buttons (Intech Laboratories, Inc., USA) with one port, no catheter implanted.
   Some caps were camouflaged with a less obvious colour and some had a bit- ter tasting additive. It seemed to make no difference. If caps fell off it was mainly due to lack of magnetic adhesion or intensive movement.

   In the group housing study no complications were noted. Behavior of the pigs showed that group housing can be an option; however some of the caps fell off, leaving the ports unprotected. For the main study the caps were modified with two magnets, but that was still not satisfactory. Further modification by adding a lock screw bracket, however not in all cases. The pigs do not interfere with the button itself but unprotected ports are not ideal. Technically a screw cap would solve the problem but they are not available from the supplier.

3. Main Study
   Increased animal number applying results from pilot. (ongoing)
   16 Göttlingen Minipigs (10–12 kg). 8 males, 8 females. With Rat Vascular Access Buttons of one port/catheter, 8 with Buttons of two ports/catheter.

   The left external jugular vein was dissected and after ligation one or two 3Fr PU catheters were 7 cm inserted if there was two catheter the insertion was through the same puncture and insertion length was 7 and 9 cm.
   Catheters were secured around the vessel with a modified Miller knot, followed by square knots. Another tie crani- al of the knot was placed as the catheter was further secured with the ends of the initial ligature incision closed in three layers using PDS II, continuous pattern, the last intradermal. (green)

   In the main study the incisions in the neck and at the site of the button healed well and no signs of infection were initially observed.

   Four weeks post surgery we found some infections around the button in 6 cases, 3 of them were minor and disap- peared quickly after treating with antibiotics. One remained an bit longer and two animals were euthanized (5 and 6 weeks after surgery) as the button was no longer embedded thoroughly in the tissue.
   Necropsy showed that the infection was limited around the button with a folded up Dracoon cuff. It might have been due to improper implantation in the fat rather than below the fat layer. The tip of the catheter was where it was supposed to be, in the vena cava and no signs of clots or thrombi were observed.

   All catheters were sent out in compliance with current laboratory guidelines for post mortem and the project was considered/not approved by the Danish Animal Experiments Inspectorate according to Danish law.

   Results of 8 weeks testing. S=slow withdraw, R=run after raising, B=blocked even after raising

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<tr>
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   Conclusion and Discussion:

   It can be concluded that Rat Vascular Access Buttons™ can successfully be implanted in Minipigs and provide long term vas- cular access. The buttons can accommodate 1-3 catheters which gives the opportunity to infuse and sample through the main unit without cross-contamination. Implantation is a permanent procedure, catheters can be explanted but this is not possible for the VAB as it is ingrown.
   Infection around the VAB can possibly be reduced by making sure the Dracoon cuff rests between the muscle and the fat layer and the skin is snug around the neck of the VAB.
   Accessing is painless and if the Minipigs are trained to be in a sling, only one person is required to perform procedures.

   There are typical catheter related issues, that can be minimized by proper catheter handling, namely locking under positive pressure.

   Preliminary results of the main study show, that the assumed advantage of having two catheters (having a backup if one is blocked) is not necessary true. Blocked catheters can become patent again after some time or repositioning the animal.